2/18/04

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims 87-164

Claims 1-86. (Cancelled)

87. (New) A DNA which upon transcription produces an RNA encoding a modified HIV-1 gp140 polypeptide, which polypeptide upon cleavage produces a modified gp120 and a modified ectodomain of gp41 which together form a complex exhibiting enhanced binding to HIV-1 neutralizing antibodies and reduced binding to HIV-1 non-neutralizing antibodies, wherein the modifications comprise an A492C mutation in gp120 and a T596C mutation in gp41, said mutations being numbered by reference to the HIV-1 isolate JR-FL, and resulting in a disulfide bond between gp120 and ectodomain gp41 which stabilizes the otherwise non-covalent gp120-gp41 interaction.

88. (New) The DNA of claim 87, wherein the HIV-1 isolate represents a subtype selected from the group consisting of clades A, B, C, D, E, F, G, H and O.

89. (New) The DNA of claim 88, wherein the HIV-1 isolate is $HIV\text{-}1_{JR\text{-}FL}$, $HIV\text{-}1_{DH123}$, $HIV\text{-}1_{GUN\text{-}1}$, $HIV\text{-}1_{89.6}$ or $HIV\text{-}1_{HXB2}$.

I. DNA 87-96, 111-113, 126-135, 150-152 536/29.72
II. VECTOR 97-104, 136-143
III. CELL 105-110, 144-149
IV. COMPLEX 114-116, 153, 155
V. MAMMALIAN COMPLEX 115, 154
VI. 6 VACCINE DNA 117-119, 122-124, 156-158, 161-163
VII. 7 VACCINE COMPLEX 120-121, 159, 160
VIII. 8 VAC VECTOR ENZ 122-124, 161-163
9 VAC DNA+PROT 126, 164

1-4, 6-9 OR 445 PROD/MM

90. (New) The DNA of claim 87, wherein the modified gp120 is further characterized by the absence of one or more of the variable loops present in unmodified gp120.

91. (New) The DNA of claim 90, wherein the absent variable loop comprises V1, V2, V3 or a combination thereof.

92. (New) The DNA of claim 90, wherein the absent variable loop comprises V1 and V2.

93. (New) The DNA of claim 87, wherein the modified gp120 is further characterized by the absence or presence of one or more canonical glycosylation sites present or absent, respectively, in unmodified gp120.

94. (New) The DNA of claim 93, wherein one or more canonical glycosylation sites are absent from the V1V2 region of the gp120.

95. (New) The DNA of claim 87, which is cDNA or genomic DNA.

96. (New) The DNA of claim 87, wherein codon usage is optimized within said DNA to enhance the translation of codons in mammalian cells.

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97. (New) A non-replicating viral vector comprising the DNA of claim 87.

98. (New) A replicable vector comprising the DNA of claim 87.

99. (New) The replicable vector of claim 98, wherein the vector is a plasmid, cosmid, virus, viral vector, λ phage or YAC.

100. (New) The replicable vector of claim 98, wherein the vector is a plasmid.

101. (New) The replicable vector of claim 99, wherein the vector is a viral vector.

102. (New) A replicable vector comprising the DNA of claim 87, wherein the modified gp120 is further characterized by the absence of one or more of the variable loops present in unmodified gp120.

103. (New) The replicable vector of claim 102, wherein the absent variable loop comprises V1, V2, V3 or a combination thereof.

104. (New) The vector of claim 102, wherein the absent variable loop comprises V1 and V2.

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105. (New) A host cell comprising the vector of claim 98.

106. (New) The cell of claim 105, which is a eukaryotic cell.

107. (New) The cell of claim 106, which is a mammalian cell.

108. (New) The cell of claim 107, which is a Chinese hamster ovary (CHO) cell.

109. (New) The cell of claim 105, which is a bacterial cell.

110. (New) The cell of claim 105, further comprising a vector which expresses an endoprotease of the furin family.

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111. (New) A composition comprising the DNA of claim 87.

112. (New) The composition of claim 111, wherein the composition comprises the DNA in a DNA plasmid, a replicating viral vector, or a non-replicating viral vector.

113. (New) The composition of claim 112, further comprising an adjuvant.

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114. (New) A modified gp120-gp41 complex which exhibits enhanced binding to HIV-1 neutralizing antibodies and reduced binding to HIV-1 non-neutralizing antibodies, wherein said modified gp120-gp41 complex is produced upon cleavage of the modified gp140 polypeptide encoded by the DNA of claim 87.

115. (New) A process for making a modified gp120-gp41 complex which exhibits enhanced binding to HIV-1 neutralizing antibodies and reduced binding to HIV-1 non-neutralizing antibodies, which process comprises:

(a) culturing the host cell of claim 105 so as to express a gp140 polypeptide which upon cleavage produces a modified gp120 and a modified ectodomain of gp41, which together form a complex; and

(b) recovering the modified gp120-gp41 complex.

116. (New) A trimer comprising a noncovalent oligomer of three identical gp120-gp41 complexes of claim 114.

117. (New) A vaccine comprising the DNA of claim 87.

118. (New) A vaccine comprising a therapeutically effective amount of the DNA of claim 87.

119. (New) A vaccine comprising a prophylactically effective amount of the DNA of claim 87.

120. (New) A vaccine comprising a therapeutically effective amount of the modified gp120-gp41 complex of claim 113.

121. (New) A vaccine comprising a prophylactically effective amount of the modified gp120-gp41 complex of claim 114.

122. (New) A vaccine comprising the DNA of any one of claims 88-104.

123. (New) A vaccine comprising a therapeutically effective amount of the DNA of any one of claims 88-104.

124. (New) A vaccine comprising a prophylactically effective amount of the DNA of any one of claims 88-104.

125. (New) A vaccine comprising a combination of the DNA of claim 87 and the modified gp120-gp41 complex of claim 114.

126. (New) A DNA which upon transcription produces an RNA encoding a modified HIV-1 gp140 polypeptide, which polypeptide upon cleavage produces a modified gp120 and a modified ectodomain of gp41 which together form a complex exhibiting enhanced binding to HIV-1 neutralizing antibodies and reduced binding to HIV-1 non-neutralizing antibodies, wherein the modifications comprise a mutation in gp120 selected from the group consisting of V35C, Y39C, W44C, P484C, G486C, A488C, P489C, T490C, and A492C and a mutation in ectodomain gp41 selected from the group consisting of D580C, W587C, T596C, V599C, P600C and W601C, said mutations being numbered by reference to the HIV-1 isolate JR-FL, and resulting in a disulfide bond between gp120 and ectodomain gp41 which stabilizes the otherwise non-covalent gp120-gp41 interaction.

127. (New) The DNA of claim 126, wherein the HIV-1 isolate represents a subtype selected from the group consisting of clades A, B, C, D, E, F, G, H and O.

128. (New) The DNA of claim 127, wherein the HIV-1 isolate is HIV-1_{JR-FL}, HIV-1_{DH123}, HIV-1_{GUN-1}, HIV-$1_{89.6}$ or HIV-1_{HXB2}.

129. (New) The DNA of claim 126, wherein the modified gp120 is further characterized by the absence of one or more of the variable loops present in unmodified gp120.

130. (New) The DNA of claim 129, wherein the absent variable loop comprises V1, V2, V3 or a combination thereof.

131. (New) The DNA of claim 129, wherein the absent variable loop comprises V1 and V2.

132. (New) The DNA of claim 126, wherein the modified gp120 is further characterized by the absence or presence of one or more canonical glycosylation sites present or absent, respectively, in unmodified gp120.

133. (New) The DNA of claim 132, wherein one or more canonical glycosylation sites are absent from the V1V2 region of the gp120.

134. (New) The DNA of claim 126, which is cDNA or genomic DNA.

135. (New) The DNA of claim 126, wherein codon usage is optimized within said DNA to enhance the translation of codons in mammalian cells.

136. (New) A non-replicating viral vector comprising the DNA of claim 126.

137. (New) A replicable vector comprising the DNA of claim 126.

138. (New) The replicable vector of claim 137, wherein the vector is a plasmid, cosmid, virus, viral vector, λ phage or YAC.

139. (New) The replicable vector of claim 137, wherein the vector is a plasmid.

140. (New) The replicable vector of claim 138, wherein the vector is a viral vector.

141. (New) A replicable vector comprising the DNA of claim 126, wherein the modified gp120 is further characterized by the absence of one or more of the variable loops present in unmodified gp120.

142. (New) The replicable vector of claim 141, wherein the absent variable loop comprises V1, V2, V3 or a combination thereof.

143. (New) The vector of claim 141, wherein the absent variable loop comprises V1 and V2.

144. (New) A host cell comprising the vector of claim 137.

145. (New) The cell of claim 144, which is a eukaryotic cell.

146. (New) The cell of claim 145, which is a mammalian cell.

147. (New) The cell of claim 146, which is a Chinese hamster ovary (CHO) cell.

148. (New) The cell of claim 144, which is a bacterial cell.

149. (New) The cell of claim 144, further comprising a vector which expresses an endoprotease of the furin family.

150. (New) A composition comprising the DNA of claim 126.

151. (New) The composition of claim 150, wherein the composition comprises the DNA in a DNA plasmid, a replicating viral vector, or a non-replicating viral vector.

152. (New) The composition of claim 150, further comprising an adjuvant.

153. (New) A modified gp120-gp41 complex which exhibits enhanced binding to HIV-1 neutralizing antibodies and reduced binding to HIV-1 non-neutralizing antibodies, wherein said modified gp120-gp41 complex is produced upon cleavage of the modified gp140 polypeptide encoded by the DNA of claim 126.

154. (New) A process for making a modified gp120-gp41 complex which exhibits enhanced binding to HIV-1 neutralizing antibodies and reduced binding to HIV-1 non-neutralizing antibodies, which process comprises:

(a) culturing the host cell of claim 144 so as to express a gp140 polypeptide which upon cleavage produces a modified gp120 and a modified ectodomain of gp41, which together form a complex; and

(b) recovering the modified gp120-gp41 complex.

155. (New) A trimer comprising a noncovalent oligomer of three identical gp120-gp41 complexes of claim 153.

156. (New) A vaccine comprising the DNA of claim 126.

157. (New) A vaccine comprising a therapeutically effective amount of the DNA of claim 126.

158. (New) A vaccine comprising a prophylactically effective amount of the DNA of claim 126.

159. (New) A vaccine comprising a therapeutically effective amount of the modified gp120-gp41 complex of claim 153.

160. (New) A vaccine comprising a prophylactically effective amount of the modified gp120-gp41 complex of claim 153.

161. (New) A vaccine comprising the DNA of any one of claims 127-143.

162. (New) A vaccine comprising a therapeutically effective amount of the DNA of any one of claims 127-143.

163. (New) A vaccine comprising a prophylactically effective amount of the DNA of any one of claims 127-143.

164. (New) A vaccine comprising a combination of the DNA of claim 125 and the modified gp120-gp41 complex of claim 153.